

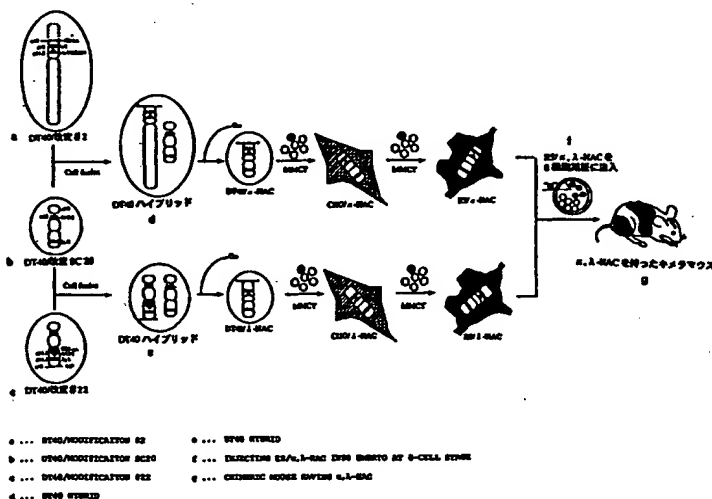


<p>(51) 国際特許分類6 A01K 67/027, C12N 5/10, 15/06</p>	<p>A1</p>	<p>(11) 国際公開番号 WO00/10383</p> <p>(43) 国際公開日 2000年3月2日(02.03.00)</p>
<p>(21) 国際出願番号 PCT/JP99/04518</p> <p>(22) 国際出願日 1999年8月23日(23.08.99)</p> <p>(30) 優先権データ 特願平10/236169 1998年8月21日(21.08.98) JP</p> <p>(71) 出願人 (米国を除くすべての指定国について) 麒麟麦酒株式会社 (KIRIN BEER KABUSHIKI KAISHA)[JP/JP] 〒104-8288 東京都中央区新川二丁目10番1号 Tokyo, (JP)</p> <p>(72) 発明者 ; および (75) 発明者 / 出願人 (米国についてのみ) 富塚一磨(TOMIZUKA, Kazuma)[JP/JP] 吉田 均(YOSHIDA, Hitoshi)[JP/JP] 石田 功(ISHIDA, Isao)[JP/JP] 黒岩義巳(KUROIWA, Yoshimi)[JP/JP] 〒370-1295 群馬県高崎市宮原町3番地 麒麟麦酒株式会社 医薬探索研究所内 Gunma, (JP) 花岡和則(HANAOKA, Kazunori)[JP/JP] 〒228-8555 神奈川県相模原市北里1-15-1 北里大学理学部生物科学科内 Kanagawa, (JP)</p>		<p>押村光雄(OSHIMURA, Mitsuo)[JP/JP] 〒683-8503 鳥取県米子市西町86 鳥取大学医学部生命科学科内 Tottori, (JP)</p> <p>(74) 代理人 平木祐輔, 外(HIRAKI, Yusuke et al.) 〒105-0001 東京都港区虎ノ門1丁目17番1号 虎ノ門5森ビル3階 Tokyo, (JP)</p> <p>(81) 指定国 AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, 欧州特許 (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI特許 (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG), ARIPO特許 (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), ユーラシア特許 (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM)</p> <p>添付公開書類 国際調査報告書</p>

(54)Title: METHOD FOR MODIFYING CHROMOSOMES

(54)発明の名称 染色体の改変方法

25



(57) Abstract

A cell having a modified foreign chromosome (fragment) is constructed by transferring the foreign chromosome into a cell having a high homologous recombination efficiency by the microcell fusion method, marking a desired site of the foreign chromosome by the homologous recombination method, and inducing deletion and/or translocation at the marked site. A method for constructing a nonhuman animal having a modified foreign chromosome (fragment) by using the above procedure; and a modified animal, a recombinant chromosome (fragment) and an artificial chromosomal vector each obtained thereby.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP99/04518

## A. CLASSIFICATION OF SUBJECT MATTER

Int.Cl<sup>6</sup> A01K 67/027, C12N 5/10, C12N 15/06

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Int.Cl<sup>6</sup> A01K 67/027, C12N 5/10, C12N 15/06

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
BIOSIS (DIALOG), JOIS (JICST)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	Tomizuka K., et al., Nature Genetics, vol.16, p.133-143 (1997)	68,70 26-67,69,71-83
X Y	WO, 97/07671, A1 (Kirin Brewery Company, limited), 06 March, 1997 (06.03.97) & AU, 6837696, A1 & EP, 843961, A1	68,70 26-67,69,71-83
Y	Dieken E.S. et al., Nature Genetics, vol.12, p.174-182 (1996)	1-92
Y	Smith A.J.H. et al., Nature Genetics, vol.8, p.376-385 (1995)	1-92
Y	Willmut et al., Nature, vol.385, p.810 (1997)	46-67
A	Ramirez-Solis R. et al., Nature, vol.378, p.720-724 (1995)	1-92
A	Mills W. et al., Human Mol.Gen., vol.8, p.751-761 (1999)	1-92



Further documents are listed in the continuation of Box C.



See patent family annex.

\* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance  
 "E" earlier document but published on or after the international filing date  
 "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)  
 "O" document referring to an oral disclosure, use, exhibition or other means  
 "P" document published prior to the international filing date but later than the priority date claimed

"T"

- later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention  
 "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone  
 "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art  
 "&" document member of the same patent family

Date of the actual completion of the international search  
15 November, 1999 (15.11.99)Date of mailing of the international search report  
24 November, 1999 (24.11.99)Name and mailing address of the ISA/  
Japanese Patent Office

Authorized officer

Facsimile No.

Telephone No.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP99/04518

## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO, 98/54348, A1 (Bruggmann M.), 03 December, 1998 (03.12.98) & GB, 97-11167, A1 & AU, 7667698, A1	1-92
A	WO, 97/49804, A1 (Baylor College of Medicine), 31 December, 1997 (31.12.97) & AU, 3507297, A1 & EP, 907726, A1	1-92

A. 発明の属する分野の分類 (国際特許分類 (IPC))		
Int. Cl. <sup>6</sup> A01K 67/027, C12N 5/10, C12N 15/06		
B. 調査を行った分野		
調査を行った最小限資料 (国際特許分類 (IPC))		
Int. Cl. <sup>6</sup> A01K 67/027, C12N 5/10, C12N 15/06		
最小限資料以外の資料で調査を行った分野に含まれるもの		
国際調査で使用した電子データベース (データベースの名称、調査に使用した用語)		
BIOSIS (DIALOG), JOIS (JICSTファイル)		
C. 関連すると認められる文献		
引用文献の カテゴリー*	引用文献名 及び一部の箇所が関連するときは、その関連する箇所の表示	関連する 請求の範囲の番号
X Y	Tomizuka K., et al., Nature Genetics, vol.16, p.133-143 (1997)	68, 70 26-67, 69, 71-83
X Y	WO, 97/07671, A1 (麒麟麦酒株式会社), 06.3月.1997 (06.03.97) & AU, 6837696, A1 & EP, 843961, A1	68, 70 26-67, 69, 71-83
Y	Dieken E.S. et al., Nature Genetics, vol.12, p.174-182 (1996)	1-92
Y	Smith A.J.H. et al., Nature Genetics, vol.8, p.376-385 (1995)	1-92
<input checked="" type="checkbox"/> C欄の続きにも文献が列挙されている。 <input type="checkbox"/> パテントファミリーに関する別紙を参照。		
* 引用文献のカテゴリー 「A」 特に関連のある文献ではなく、一般的技術水準を示すもの 「E」 国際出願日前の出願または特許であるが、国際出願日以後に公表されたもの 「L」 優先権主張に疑義を提起する文献又は他の文献の発行日若しくは他の特別な理由を確立するために引用する文献 (理由を付す) 「O」 口頭による開示、使用、展示等に言及する文献 「P」 国際出願日前で、かつ優先権の主張の基礎となる出願日の後に公表された文献 「T」 国際出願日又は優先日後に公表された文献であって出願と矛盾するものではなく、発明の原理又は理論の理解のために引用するもの 「X」 特に関連のある文献であって、当該文献のみで発明の新規性又は進歩性がないと考えられるもの 「Y」 特に関連のある文献であって、当該文献と他の1以上の文献との、当業者にとって自明である組合せによって進歩性がないと考えられるもの 「&」 同一パテントファミリー文献		
国際調査を完了した日	15. 11. 99	国際調査報告の発送日
国際調査機関の名称及びあて先 日本国特許庁 (ISA/J P) 郵便番号100-8915 東京都千代田区霞が関三丁目4番3号		特許庁審査官 (権限のある職員) 長 井 啓 子 印 電話番号 03-3581-1101 内線 3236

C (続き) . 関連すると認められる文献		
引用文献の カテゴリー*	引用文献名 及び一部の箇所が関連するときは、その関連する箇所の表示	関連する 請求の範囲の番号
Y	Willmut et al., Nature, vol.385, p.810 (1997)	46-67
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A	Mills W. et al., Human Mol.Gen., vol.8, p.751-761 (1999)	1-92
A	WO, 98/54348, A1 (Bruggmann M.), 03.12月.1998 (03.12.98) & GB, 97-11167, A1 & AU, 7667698, A1	1-92
A	WO, 97/49804, A1 (Baylor College of Medicine), 31.12月.1997 (31.12.97) & AU, 3507297, A1 & EP, 907726, A1	1-92

Derwent abstract of WO 2000/10383

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DIALOG(R)File 351:Derwent WPI

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WPI Acc No: 2000-246479/200021

XRAM Acc No: C00-074558

XRPX Acc No: N00-184366

Producing a cell containing modified foreign chromosomes, useful for the generation of transgenic animals

Patent Assignee: KIRIN BEER KK (KIRI )

Inventor: HANAOKA K; ISHIDA I; KUROIWA Y; OSHIMURA M; TOMIZUKA K; YOSHIDA H

Number of Countries: 089 Number of Patents: 003

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
WO 200010383	A1	20000302	WO 99JP4518	A	19990823	200021 B
AU 9953042	A	20000314	AU 9953042	A	19990823	200031
EP 1106061	A1	20010613	EP 99938578	A	19990823	200134
			WO 99JP4518	A	19990823	

Priority Applications (No Type Date): JP 98236169 A 19980821

Patent Details:

Patent No Kind Lan Pg Main IPC Filing Notes

WO 200010383 A1 J 316 A01K-067/027

Designated States (National): AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW

Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW

AU 9953042 A A01K-067/027 Based on patent WO 200010383

EP 1106061 A1 E A01K-067/027 Based on patent WO 200010383

Designated States (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

Abstract (Basic): WO 200010383 A1

NOVELTY - Producing cells (I) containing a modified foreign chromosome or chromosome fragment, is new.

DETAILED DESCRIPTION - The method of (I) comprises:

(a) fusing a microcell comprising the foreign chromosome or chromosome fragment, with a cell having a high efficiency for homologous recombination;

(b) marking the desired site of insertion of the foreign chromosome using a targeting vector; and

(c) inducing deletion or translocation at the marked site.

INDEPENDENT CLAIMS are also included for the following:

(1) cells containing a foreign chromosome or chromosome fragment;

(2) producing a non-human chimeric animal containing cells as in

(1); and

(3) targeting vectors (including artificial chromosome vectors) for use in (2).

USE - The transgenic animals produced are useful to provide disease models and knockout animals, and in the production of human proteins, particularly human antibodies.

DESCRIPTION OF DRAWING(S) - The drawing is a diagrammatic

representation of the production of a chimeric mouse.

pp; 316 DwgNo 55/71

Technology Focus:

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Cells: The cell having a high efficiency for homologous recombination is an animal cell, such as chicken DT40 cells or mammalian embryonic stem cells. Preferred Vector: The targeting vector contains a partially deleted telomere sequence and is bound to an enzyme such as Cre enzyme, which targets a template sequence such as loxP to induce deletion and/or recombination.

Preferred Method: Cells in which deletion and/or recombination has occurred can be selected using a marker gene such as a drug resistance gene or green fluorescent protein gene.

Preferred Organisms: Transgenic animals produced using the cells containing a foreign chromosome or chromosome fragment include mammals e.g. mouse, sheep and cattle, and birds e.g. chickens.

Title Terms: PRODUCE; CELL; CONTAIN; MODIFIED; FOREIGN; CHROMOSOME; USEFUL; GENERATE; TRANSGENIC; ANIMAL

Derwent Class: B04; D16; P14

International Patent Class (Main): A01K-067/027

International Patent Class (Additional): C12N-005/10; C12N-015/06

File Segment: CPI; EngPI

Manual Codes (CPI/A-N): B04-E02; B04-E02A; B04-E08; B04-F0200E; B04-F0700E; B04-L01; B04-P01A0E; B04-P01B0E; D05-H12A; D05-H12B; D05-H12E; D05-H14B2; D05-H14B4; D05-H16A; D05-H17A1; D05-H17B1

Chemical Fragment Codes (M1):

\*01\* M423 M710 M720 M905 N104 N135 N136 N137 Q233 RA00GT-N RA00GT-P

\*02\* M423 M710 M905 N135 Q233 RA00NS-N

\*03\* M423 M710 M905 N135 Q233 RA012P-N

Specific Compound Numbers: RA00GT-N; RA00GT-P; RA00NS-N; RA012P-N

Key Word Indexing Terms:

\*01\* 200757-0-0-0-CL, NEW, PRD 93605-0-0-0-CL, NEW 105730-0-0-0-CL, NEW

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